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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/12/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/821,726	MARTIN ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *12,16-21 and 23-26* is/are withdrawn from consideration.

5)☒ Claim(s) *7-11* is/are allowed.

6)☒ Claim(s) *1-6,13-15,22 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to the "Amendment and Response..." filed 5 February 2003 (Paper No. 18) in reply to the Non-Final Office Action mailed 3 October 2002 (Paper No. 16). Claims 12, 16-21 and 23-26 were withdrawn from consideration and claims 1-11, 13-15, 22 and 27-29 were considered in Paper No. 16. Claims 1-4 and 7-11 were amended in Paper No. 18.

Response to Amendment

Claim Objections

Objection to claims 2-4 and 7-10 is withdrawn.

Claim Rejections - 35 USC § 112, 1st Paragraph

Rejection of claims 1, 5, 6, 11 13-15, 22 and 27-29 under 35 U.S.C. 112, first paragraph, as lacking adequate written description is withdrawn.

Rejection of claims 1, 5, 6, 11, 13-15, 22 and 27-29 under 35 U.S.C. 112, first paragraph, as lacking enablement for a protein or method of using a protein comprising the amino acid sequence VKE*X*KKXXGKGPGGXPPK or VKE*Q*KK*XX*GKGPGG*X*PPK is withdrawn.

Claims 13-15, 22 and 27-29 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for reasons of record in Paper No. 16 and herein below in the "Response to Arguments".

Claim Rejections - 35 USC § 112, 2nd Paragraph

Claims 1, 5, 13-15, 22 and 27-29 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite in being drawn to a products and methods comprising a group of isolated *homologous* cellular growth stimulating proteins for reasons of record in Paper No. 16 and herein below in the "Response to Arguments".

Rejection of claims 2, 3, 4, 6 and 7-11 under 35 U.S.C. § 112, second paragraph, for reasons of record in Paper No. 16 is withdrawn.

Claim Rejections - 35 USC § 102

Claim 4 stands rejected under 35 U.S.C. 102(a) as anticipated by Hayashizaki *et al.* (8 February 2001) *Nature* 409:685-690 for reasons of record in Paper No. 16 and herein below in the "Response to Arguments".

Claim 2 stands rejected under 35 U.S.C. 102(b) as anticipated by Powell (1987) IDS #BQ for reasons of record in Paper No. 16 and herein below in the "Response to Arguments".

Rejection of claims 3 and 11 under 35 U.S.C. 102 as anticipated by the art of record is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 112, 1st Paragraph

Claims 13-15, 22 and 27-29 were rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for pharmaceutical compositions and methods of treatment comprising the disclosed polypeptides. In response, Applicant cites *Cross v. Iuzuka*, 753 F.2d 1040 1050, 224 USPQ 739, 747 (Fed. Cir. 1985) and argues, "[i]t is well known in the art that *in vitro* cell culture studies convey a reasonable prediction for *in vivo* activities. A rigorous or an invariable correlation is not required" (page 5). However, it is important to keep in mind that in *Cross v. Iuzuka* the Court was careful to distinguish claims directed to compounds from claims directed to therapeutic use. At page 748, the Court states, "[t]his is not a case such as *In re Gardner*, 427 F.2d 786, 166 USPQ 138 (1970), where the CCPA held that the applicant's disclosure was nonenabling because inventive skill and undue experimentation would be required to discover approprite [sic] dosages for humans, *i.e., a therapeutic use*. In the instant case, we are confronted with a pharmacological activity or practical utility, not a therapeutic use." (emphasis added). Thus, the Court in *Cross v. Iuzuka* indicates that claims directed to therapeutic use are addressed by *In re Gardener*. In *In re Gardener,* the Court found that claims directed to methods of treatment or compositions claimed in terms of use are not enabled in the absence of a clear teaching of how the compositions or methods can be effectively used for the purpose set forth in the specification. Specifically, the teachings of Gardner were found inadequate to support claims directed to therapeutic use of an antidepressant composition because they failed to provide an effective dosage regimen. As stated in the previous office action, "[t]he disclosure provides no guidance as to how a AMP-18 peptide or protein, or inhibitor thereof, should be administered, or how much should be administered, in order to achieve a therapeutic effect" (bridging pages 8-9).

Therefore, the instant disclosure is not enabling for the claims, at least, for the same reasons that the claims of Gardner were not enabled.

Applicant also cites MPEP 2164.05, which indicates that considerations made by the FDA for approving clinical trials are different from those made by the PTO in determining whether a claim is enabled. Applicant's point is taken inasmuch as enablement does not require demonstration of safety or efficacy. However, the disclosure must teach the skilled artisan how to use the claimed subject matter and, "[u]nless and until a process is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field" (see *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 at 695). The previous office action cites several teachings from the art that indicate a high degree of unpredictability in refining the claimed compositions and methods such that specific benefit exists. Given this unpredictability and the absence of teachings specifically directed to treatment using the disclosed polypeptide, the skilled artisan would not be able to practice the claimed invention without first engaging in undue experimentation.

Next, Applicant argues that the specification discloses that AMP-18 structural domains resemble the anti-microbial magainins and thus AMP-18 may interfere with *H. pylori*. However, the specification provides no evidence of antimicrobial activity for the claimed polypeptide. Furthermore, the same passage to which Applicant refers also speculates that AMP-18 might be a tropic factor for *H. pylori*. Therefore, the teachings amount to general speculation on what AMP-18 might do and not a specific teaching of a treatment method.

Finally, Applicant argues that disclosure of AMP-receptor expression is not relevant to practice the present invention because the localization of AMP-18 protein in the antrum mucosal tissue was disclosed in the specification and the knowledge of AMP-18 expression will guide the artisan to design appropriate treatment methods. This argument is not persuasive because the statement cited by Applicant was provided as one of many reasons for unpredictability in developing an effective treatment for any disease according to the teachings of the instant disclosure. When viewed as a whole, the teachings from the prior art cited in the previous office action clearly indicate that a simple teaching of where AMP-18 is expressed *in vivo* would not enable the skilled artisan to treat any disease using the claimed methods or compositions without engaging in undue experimentation.

Thus, for reasons of record and herein above, the claims stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an enabling disclosure.

Claim Rejections - 35 USC § 112, 2nd Paragraph

In response to rejection of claims 1, 5, 13-15, 22 and 27-29 as indefinite in being drawn to a products and methods comprising a group of isolated *homologous* cellular growth stimulating proteins, Applicant argues that the meaning of the claim is sufficiently clear from the standard definition of homology. However, as indicated by the definition provided on page 7 of Paper No. 18, homology is a term of measure. Without some limitation of degree, it is unclear what constitutes a "homologous" protein. That is, at what point is a protein produced by gastric epithelial cells and comprising the amino acids in the sequence VEKEK/QKXXGKGPGGXPPK

no longer homologous. This rejection could be overcome by removing the word "homologous" from the claim.

Claim Rejections - 35 USC § 102

Claim 4 was rejected under 35 U.S.C. 102(a) as anticipated by Hayashizaki *et al.* (8 February 2001) *Nature* 409:685-690. In response to the rejection of record, Applicant has amended the claim such that it is directed to the processed form of the mouse AMP-18 protein that lacks the signal peptide. However, because the claimed protein is open (i.e., directed to a protein comprising SEQ ID NO: 16) the polypeptide of Hayashizaki *et al.*, which comprises the claimed portion of AMP-18, reads on the claim.

Claim 2 was rejected under 35 U.S.C. 102(b) as anticipated by Powell (1987) IDS #BQ. In response to the rejection of record, Applicant argues that the amended claim 2 relates to a processed form of pig AMP-18 protein having 165 amino acids that lacks the signal peptide, while Powell teaches a 185 amino acid sequence. This argument is not persuasive because, as with claim 4, the protein claimed in claim 2 reads on any protein which comprises the amino acid sequence from positions 21-185 of SEQ ID NO: 18. The claimed protein is additionally limited to a protein that is present in pig gastric epithelia in a processed form lacking the 20 amino acids which constitute a signal peptide sequence, having 165 amino acids and an estimated molecular weight of approximately 18 kD as measured by polyacrylamide gel electrophoresis and capable of being secreted. However, because Powell teaches a pig AMP-18, each of these limitations

would be inherent to the protein as it is found in pig gastric epithelia. Thus, the protein taught by Powell meets the limitations of claim 2.

New Grounds Necessitated by Amendment

Claim Objections

Claim 1 is objected to because Applicant did not supply a clean copy of the claim. SEQ ID NO: 1 appears in the claim as VKEK/QK[K]XXGKGPGGXPPK.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 2 has been amended such that it is now limited to a protein comprising positions 21 to 185 of SEQ ID NO: 18. There is no support for a protein specifically limited to comprising positions 21 to 185 of SEQ ID NO: 18 in the originally filed specification and claims.

Claims 1, 3-6, 13-15, 22 and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a protein, and methods of using said protein, comprising "the amino acids in the sequence" set forth in the claims. The claims as written do not require the claimed proteins comprise the amino acids in the sequence set forth in the disclosed order. Therefore, the claims encompass any protein that comprises the amino acids set forth, in any order and in non-contiguous form. That is, the claimed protein need only comprise the amino acids *in* the sequence, not the amino acid sequence. Thus, the claims are directed to a genus of proteins of essentially unlimited structure and having the function of a gastrokine. An adequate written description of a protein requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the protein itself. It is not sufficient to define protein solely by its principal biological property, i.e., it has the function of a gastrokine, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any protein with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all proteins that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). With respect to the method claims, adequate description of the

methods first requires an adequate description of the materials, i.e. specific protein sequences, which provide the means for practicing the invention.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of proteins having the function of a gastrokine. Therefore, only the described proteins comprising the sequence set forth in the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Hayashizaki *et al.* (8 February 2001) *Nature* 409:685-690.

Hayashizaki *et al.* teaches the amino acid sequence of the mouse AMP-18 protein, which protein is a growth stimulating protein produced by gastric epithelial cells and comprises the sequence VKEQKGKGPGGAPPK. The protein of Hayashizaki *et al.* thus anticipates the limitations of claim 1.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by either one of Powell (1987) IDS #BQ or Jacobs *et al.* (1999; WO 99/07840).

Powell teaches the amino acid sequence of human and porcine AMP-18 proteins, which proteins are a growth stimulating protein produced by gastric epithelial cells and comprises the sequence VKEKKGKGPGGAPPK. Jacobs *et al.* teaches the amino acid sequence of porcine AMP-18 proteins, which protein is a growth stimulating protein produced by gastric epithelial cells and comprises the sequence VKEKKGKGPGGAPPK. The proteins of Powell and Jacobs *et al.* thus anticipate the limitations of claim 1.

Drawings

The drawings are objected to for the reasons indicated on the attached PTO-948. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. **Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Allowable Subject Matter

Claims 7-11 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
April 29, 2003

JAMES KETTER
PRIMARY EXAMINER